WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences

Search Results -

Terms	Documents
(liposomes) adj3 photosensitizer$	18

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: (liposomes) adj3 photosensitizer$ Clear

Search History

Today's Date: 1/22/2001

DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) adj3 photosensitizer$	18	L6
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) adj3 iontophoresis	49	L5
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) adj5 iontophoresis	92	L4
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) same (electrical)	133	L3
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) same (electrical or iontophore$$$)	299	L2
USPT,JPAB,EPAB,DWPI,TDBD	liposomes same (electrical or iontophore$$$)	299	L1

WEST

Generate Collection

L3: Entry 4 of 133 File: USPT Nov 21, 2000

DOCUMENT-IDENTIFIER: US 6150338 A
TITLE: Gene therapy for alleviating erectile dysfunction

DEPR:
The DNA sequence may be introduced into the smooth muscle cell by a number of procedures known to one skilled in the art, such as electroporation, DEAE Dextran, monocationic liposome fusion, polycationic liposome fusion, protoplast fusion, DNA coated microprojectile bombardment, by creation of an in vivo electrical field, injection with recombinant replication-defective viruses, homologous recombination, and naked DNA transfer. It is to be appreciated by one skilled in the art that any of the above methods of DNA transfer may be combined.

DEPR:
The introduction of the DNA sequence into the cells of the subject may be effected by methods known to one skilled in the art, such as electroporation, DEAE Dextran, cationic liposome fusion, protoplast fusion, by creation of an in vivo electrical field, DNA coated microprojectile bombardment, injection with recombinant replication-defective viruses, homologous recombination, and naked DNA transfer. It will be appreciated by those skilled in the art that any of the above methods of DNA transfer may be combined. In a preferred embodiment of the invention, DNA transfer is the preferred method.

WEST

Generate Collection

L3: Entry 7 of 133 File: USPT Oct 10, 2000

DOCUMENT-IDENTIFIER: US 6130207 A
TITLE: Cell-specific molecule and method for importing DNA into a nucleus

DEPR:
Various methods are known in the art for introducing nucleic acid molecules into host cells (including the specific cell type). One method is microinjection, in which DNA is injected directly into the cytoplasm of cells through fine glass needles. Alternatively, DNA can be incubated with an inert carbohydrate polymer (dextran) to which a positively charged chemical group (DEAE, for diethylaminoethyl) has been coupled. The DNA sticks to the DEAE-dextran via its negatively charged phosphate groups. These large DNA-containing particles stick in turn to the surfaces of cells, which are thought to take them in by a process known as endocytosis. In another method, cells efficiently take in DNA in the form of a precipitate with calcium phosphate. In electroporation, cells are placed in a solution containing DNA and subjected to a brief electrical pulse that causes holes to open transiently in their membranes. DNA enters through the holes directly into the cytoplasm, bypassing the endocytotic vesicles through which they pass in the DEAE-dextran and calcium phosphate procedures (passage through these vesicles may sometimes destroy or damage DNA). DNA can also be incorporated into artificial lipid vesicles, liposomes, which fuse with the cell membrane, delivering their contents directly into the cytoplasm. In an even more direct approach, DNA is absorbed to the surface of tungsten microprojectiles and fired into cells with a device resembling a shotgun.

L3: Entry 13 of 133 File: USPT Jul 25, 2000

DOCUMENT-IDENTIFIER: US 6093557 A
TITLE: Electrospraying apparatus and method for introducing material into cells

DEPR:
In addition to penetration of the cells as a result of the bombardment of the cells with material using the present invention, the electrospraying technique described herein may be used to produce liposome droplets encapsulating biological material, e.g., DNA. The liposome droplets can be directed by the electric field and distributed uniformly over target cells in manners similar to those described herein, e.g., movement of the target surface, movement of the distributor head, etc. As opposed to the penetration of the cells at impact, the liposomes incapsulating the biological material facilitate transfer of the material into the cells through fusion of the liposome with the cell membrane as is known to those skilled in the art. The liposome droplets may be of varying sizes, e.g., a nominal diameter of about 10 nm to about 10 .mu.m. The electrospraying technique used to direct the liposomes onto the cells can be adjusted (e.g., distance of nozzle to target surface can be adjusted, electrical potential or strength of the field can be adjusted, etc.) to vary the velocity of the liposome droplets such that the liposome droplets land appropriately for the fusion mechanism to be accomplished.

L3: Entry 25 of 133 File: USPT Mar 21, 2000

DOCUMENT-IDENTIFIER: US 6041252 A
TITLE: Drug delivery system and method

ABPL:
A method for delivering a therapeutic agent to a predetermined location in a host is disclosed, wherein a liposome-encapsulated therapeutic agent is administered to the host, and an electrical field which encompasses a predetermined region within the host is established, such that as the liposome-encapsulated agent is exposed to the electrical field the release of the agent from the liposome to the predetermined region is enhanced.

BSPR:
In one aspect, the present invention provides a method for delivering a therapeutic agent to a predetermined location in a host. The method comprises providing a liposome-encapsulated therapeutic agent to the host, establishing an electrical field which encompasses a predetermined region within the host, and exposing the liposome-encapsulated agent to the electrical field so as to enhance the release of the agent from the liposome to the predetermined region.

BSPR:
In the practice of such aspects of the present invention the release of the contents of both solid and fluid liposomes is greatly increased by exposure to high voltage transient electrical fields. It has been shown (Mueller et al. (1983) and Chang et al. (1992)) that liposomes exposed to brief external high voltage electrical fields have demonstrated the formation of pores and, above a critical voltage (E.sub.C), the liposomes will rupture. These effects can occur either at normal body temperature, over a wide range of temperatures, or through non-thermal interaction with non-ionizing electromagnetic radiation at temperatures other than T.sub.C. Thus, the present invention offers a fast and effective method for rapid release of liposome encapsulated therapeutic agents and/or other chemicals into localized areas in cells, tissues, or organs in the body of a patient.

BSPR:
In accordance with certain aspects of the invention, liposomes may be made of inexpensive materials and the drug release from these liposomes can be effected by applying to the predetermined treatment area an electrical field of intensity sufficient to effect the release of the drug from the liposomes.

DEPR:
In one aspect, the present invention provides a method for delivering a therapeutic agent to a predetermined location in a host. The method comprises providing a liposome-encapsulated therapeutic agent to the host, establishing an electrical field which encompasses a predetermined region within the host, and exposing the liposome-encapsulated agent to the electrical field so as to enhance the release of the agent from the liposome to the predetermined region.

DEPR:
"On demand" liposome release can also be obtained utilizing high voltage electrical fields similar to those found in electroporation/electropermeabilization. It has been shown (Mueller et al. (1983) and Chang et al. (1992)) that exposure to brief external high voltage fields in both solid and fluid liposomes will promote the formation of pores and, if the electrical field is high enough, effect rupture. These effects can occur either at normal body temperature or over a wide range of temperatures. The electrical fields causing electropermeabilization act to trigger drug delivery in two ways:

(1) by destabilizing the liposome bilayer so that membrane fusion between the liposome and the target cellular structure occurs, thus facilitating the direct delivery of drug into the target cell; and (2) by triggering the release of drug in high concentrations from liposomes at the surface of the target cell so that the drugs are driven across the cell membrane by a concentration gradient. In either case, the direct cellular-level microinjection of drug into the target cell is achieved.

DEPR:
A further consideration of liposome-mediated delivery relates to the potential for controlling the direction and speed of movement of charged liposomes utilizing subthreshold iontophoretic fields which are applied from the elements of the electrode array. These liposomes will contain negative external charges which should cause them to migrate through the extracellular fluid space towards the positive pole of the iontophoretic field, thus allowing differential positioning of the liposomes in vivo. In this aspect of the invention, a central electrode element in conjunction with satellite electrodes will act as confining dipoles to limit the excursion of the electrical field outside the desired area. Utilization of this aspect of the invention will allow for increased concentrations of materials in certain areas of the target body site which may have poor blood distribution, compressed cytoarchitecture, etc., features well documented in tumors.

DEPR:
A further aspect of the invention involves the directed migration of charged liposomes to certain areas of the target body site, as defined by the subthreshold iontophoretic fields applied utilizing the electrode array. The liposomes used in this aspect of the present invention will desirably contain negative charges on the outer surface, which should cause them to migrate towards the positive pole of the iontophoretic field, thus potentially allowing differential positioning of the liposomes in vivo. As a feature of this aspect of the invention, the central electrode element in conjunction with the satellite electrodes will act as confining dipoles to limit the excursion of the electrical field outside the desired area. This feature will allow for increasing the concentrations of the liposome-encapsulated materials in certain areas of the target body site which may have differential blood distribution, cytoarchitecture, etc.

DEPR:
In certain aspects, the present invention involves the preparation of drugs encapsulated in liposomes affected by electroporation pulses using very brief high voltage electrical fields. The permeability of liposome membranes depends on many factors which include their lipid composition, the type of drug, drug sequestration into the bilayer membrane or into the aqueous interior compartment, the site of release and other complex physicochemical properties. It is generally recognized that undisturbed liposomes are not very permeable, but can be made so by altering membrane properties.

DEPR:
Thus, the invention provides a novel method of placing a series of electrodes into the target body site of interest, thereby setting up geometrically-oriented electrical fields by which to perform electroporation. As an adjunct to the electroporation, liposomes encapsulating various compounds, and designed to maximize the effect of electroporation pulses and deliver drugs to diseased tissues are also utilized and methods are described to iontophoretically localize charged liposomes.

DEPR:
The present invention desirably utilizes liposomes which possess a phase transition temperature T.sub.C within the temperature range of interest, generally several degrees below their transition (T.sub.C) temperatures. Such liposomes are referred to as phase transition liposomes which will be in the fluid (liquid) phase state following application of electroporation pulses. Drug delivery using electrical fields using liposomes at temperatures corresponding to T.sub.C have been previously described in U.S. Pat. Nos. 4,801,459 and 5,190,761.

DEPR:
Liposomes without a reverse transition over a specified temperature range can be

prepared when a suitable perturbing agent is added to the phospholipid membrane, or when a multicomponent phospholipid liposome is constructed. Thus, for example, the perturbing agent cholesterol can be added to the membrane of a liposome displaying a T.sub.C over a specified temperature range of interest. Such a membrane is comprised of, for example, a single highly purified phospholipid. At sufficient concentrations, cholesterol converts this material essentially into a nonphase transition liposome. The obliteration of a reverse transition will render liposome membranes impermeant and highly stable with regard to leakage of drug. In the method here described using electrical fields as a triggering agent for liposome drug release, one observes a significant increase in drug release from nonphase transition liposomes during treatment with electrical fields.

DEPR:
Liposomes may be administered to persons as a liposome depot at a tissue site or may be administered directly into the circulation. Circulating nonphase transition liposomes will not release the drug unless subjected to an electrical field. In turn, electrical fields may be selectively directed only to target areas where the drug release is desired. All other liposomes outside the target area will not release the drug; liposomes in the general circulation and liposomes at a distant liposome depot outside of the exposure site will remain intact until their eventual sequestration by the reticuloendothelial system in the body. The process of drug release using electrical fields may be repeated intermittently until all drug is released from the liposome population.

DEPR:
The suspension is then administered to the patient in need of treatment and the liposomes are subsequently treated with a safe but effective dose of electrical field. "Safe" in this context means that it does not heat the tissue to hyperthermic (43.degree. C.) or supra-hyperthermic (>43.degree. C.) temperature levels that may cause tissue damage.

DEPR:
The liposomes may be injected as localized depots or may be injected to circulate freely in the blood stream with the potential to be targeted to specific tissue sites and localize at a site of interest. The latter case is termed targeted drug delivery and the bound liposomes are treated with the electrical field to trigger localized drug release at the target site.

DEPR:
The electrical fields causing electroporation act to trigger drug delivery in two ways: (1) by destabilizing the liposome bilayer so that membrane fusion between the liposome and the target cellular structure occurs, thus facilitating the direct delivery of drug into the target cell; and (2) by triggering the release of drug in high concentrations from liposomes at the surface of the target cell so that the drugs are driven across the cell membrane by a concentration gradient upon via the created electropores. In either case, the direct cellular-level microinjection of drug into the target cell is achieved.

DEPR:
The electrical field source is then placed, desirably via the HexasphereTM electrode array, into the tissue of desired localization of the drug delivery. Although the liposomes are delivered systemically, with some exception, the localized field effect serves to constrain the electroporation effect to the geometrically-oriented area as defined by the electrodes. Thus, the liposomes in this area are treated and will release encapsulated drug as they circulate through this local electrical field. The patient can be treated with the field for a single treatment or be treated at different time periods (i.e. multiple doses) using a number of intermittent applications of the field.

DEPR:
The specific process of targeted drug delivery using liposomes via the present method has several unique advantages. The liposomes affinity for the target cell results in adsorption or binding to the target cell resulting in an extraordinarily high concentration of encapsulated drug at the surface of the target cell. A typical target cell has a diameter of approximately 7 .mu.m (7,000 .mu.m). This is large compared to the size of a liposome vesicle (having a typical diameter of 100 nm). Approximately 450 million liposome vesicles can be bound to the surface of such a target cell, and each liposome vesicle can be loaded with drug at a high concentration (>100 mM). This situation represents the

most effective means for bringing high concentrations of drug to the surface of a target cell. Using electrical fields via the method provided, the problem of releasing drug from these bound liposomes can be overcome.

DEPR:
Another aspect of this invention is enhancement of the conductance of the electrical field throughout the target body site utilizing liposome-encapsulated particular materials designed to allow application of similar electrical fields throughout the target body site as defined by the electrode array. Local delivery of electrically conductive solutions (e.g. ionic solutions, Fe++-containing solutions, etc.) designed to facilitate the spread of the electrical field throughout the interstitial spaces of the tissue defined by the outline of the array would assist in preconditioning the predefined region and create a more uniform field conductance, thus maximizing the electroporation effect.

DEPR:
Thus, the present invention includes the delivery of materials which will aid in the pulse conduction through the interstitial compartment. This may be accomplished utilizing liposomes or may involve the already described local delivery methods of injection followed by distribution utilizing electrical field influence upon charged particles. Alternatively, this increase in ionic strength in the interstitial fluid might be accomplished by first using liposome-mediated delivery of hypertonic materials to the tumoral or diseased sites; then at subthreshold values of E.sub.C, bring about the release of the materials which will diffuse into the interstitial medium and cause a relative increase in .lambda..sub.0. Thus, during the electroporation phase, a more effective pulse propagation will result, resulting in an increased number of cells which undergo reverse electrical breakdown.

DEPR:
This aspect of the invention relates generally to the electrokinetic mass transfer of charged molecules or liposomes to particular regions of tissue based upon the desired overall interstitial fluid distribution. It is considered desirable to have an effective way of delivering the desired compounds without risking harm to the tissue structure from direct electrical contact and to avoid exposure of healthy tissue from the effect of the iontophoretic field. Care must be taken to avoid current flow along the path of least resistance into an area of tissue weakness, resulting in a localized burn. This pattern of current flow is also known as tunneling. Current carried through the liquid reverse (interstitial fluid) is carried by ions (ionic conduction). In order for current to flow, it is necessary for electrical charge to be transferred to chemical species in solution by means of oxidation and reduction charge transfer reactions at the electrode surfaces. The Nernst-Planck equation describes the movement of ionic species in mass transport. The first term describes the flux due to passive diffusion, which is proportional to the concentration gradient of species i. The second term describes the flux due to the electromigration or electrodiffusion, where the driving force is the gradient of electrical potential. The third term describes the flux due to convection, where the mechanism of transport is the movement of material by bulk fluid flow which is determined by the magnitude and direction of the bulk fluid velocity vector:

DEPR:
In this device, the core and satellite electrodes will be used as iontophoretic devices with application of low voltage constant electrical fields across varying configurations in order to thoroughly distribute the various charged particles (including charged liposomes and other macromolecules including concentration ionic solutions for the improvement of intratumoral conductivity) throughout the tumoral or diseased tissue. DC currents in the micro to milliampere range will be utilized and the likely source of the constant current would likely be an appropriate field effect transistor and a variable resistor. These controllers are commercially available and normally consume only about 0.5-0.7 V. It is likely that there will be hindrance to high molecular weight compounds in the brain extracellular microenvironment

DEPR:
Alternatively, the use of iontophoretic or pulsed fields can be employed to influence the migration of charged liposomes within interstitial fluid, again concentrating materials in particular locations. It has been demonstrated that constant electrical fields can increase the adsorption of liposomes to cell

walls, thus increasing the likelihood of incorporation or of fusion following electroporation pulses. Also of use in this regard would be the utilization of phase transition temperature-specific liposomes for the purpose of controlled release at the appropriate temperature.

WEST

Generate Collection

L3: Entry 48 of 133 File: USPT Oct 27, 1998

DOCUMENT-IDENTIFIER: US 5827705 A
TITLE: Molecule and method for importing DNA into a nucleus

DEPR:
Various methods are known in the art for introducing nucleic acid molecules into host cells. One method is microinjection, in which DNA is injected directly into the cytoplasm of cells through fine glass needles. Alternatively, DNA can be incubated with an inert carbohydrate polymer (dextran) to which a positively charged chemical group (DEAE, for diethylaminoethyl) has been coupled. The DNA sticks to the DEAE-dextran via its negatively charged phosphate groups. These large DNA-containing particles stick in turn to the surfaces of cells, which are thought to take them in by a process known as endocytosis. In another method, cells efficiently take in DNA in the form of a precipitate with calcium phosphate. In electroporation, cells are placed in a solution containing DNA and subjected to a brief electrical pulse that causes holes to open transiently in their membranes. DNA enters through the holes directly into the cytoplasm, bypassing the endocytotic vesicles through which they pass in the DEAE-dextran and calcium phosphate procedures (passage through these vesicles may sometimes destroy or damage DNA). DNA can also be incorporated into artificial lipid vesicles, liposomes, which fuse with the cell membrane, delivering their contents directly into the cytoplasm. In an even more direct approach, used primarily with plant cells and tissues, DNA is absorbed to the surface of tungsten microprojectiles and fired into cells with a device resembling a shotgun.

WEST

Generate Collection

L3: Entry 50 of 133 File: USPT Sep 29, 1998

DOCUMENT-IDENTIFIER: US 5814008 A
TITLE: Method and device for applying hyperthermia to enhance drug perfusion and efficacy of subsequent light therapy

DEPR:
In FIG. 1, a syringe 16 coupled to a needle 18 is illustrated in a position for infusing the photoreactive agent into tumor 12. It is also contemplated that the photoreactive agent can be delivered to tumor 12 in other ways, such as by a general infusion of the reagent into a patient's vascular system, orally, or by delivery through a lumen of a catheter coupled to PDT probe 14; the electrical leads attached to probe 14 are generally represented by a line 15 in FIG. 1. Alternatively, a heat sensitive drug carrier such as a liposome or a polymer can carry the drug to the treatment site so that when the treatment site is heated by the PDT probe, the drug carrier releases the drug into the treatment site so that the drug infuses throughout the tissue at the site.

WEST

Generate Collection

L3: Entry 97 of 133 File: USPT Apr 19, 1994

DOCUMENT-IDENTIFIER: US 5304486 A
TITLE: Method of and apparatus for cell portion and cell fusion using radiofrequency electrical pulse

ABPL:
Disclosed are an apparatus and a method for the poration and fusion of cells using high-power radiofrequency electrical pulses. The electrodes of the apparatus can be hand held or part of integrated equipment with special containers for cells. The electrodes, which are positioned equidistant from each other, are attached to a high power function generator. The power function generator can apply a continuous AC electrical field and/or a high-power pulsed radiofrequency electrical field across the electrodes. The alternating electrical field induces cell congregation by the process of dielectrophoresis. The high-power pulsed radiofrequency electrical field porates or fuses the cells. The method has the ability to porate or fuse biological cells with a very high efficiency. The method can be used to fuse or porate a variety of cells including animal cells, human cells, plant cells, protoplasts, erythrocyte ghosts, liposomes, vesicles, bacteria and yeasts. The method has the unique ability to porate or fuse cells in very small or very large numbers. During the poration or fusions, a variety of chemical agents including DNA, RNA, antibodies, proteins, drugs, molecular probes, hormones, growth factors, enzymes, organic chemicals and inorganic chemicals can be introduced into these cells. The method can also be used to produce new biological species, to make hybridoma cells which produce animal or human monoclonal antibodies and to insert therapeutic genes into human cells which can be transplanted back into the human body to cure genetic diseases.

WEST

Generate Collection

L3: Entry 108 of 133 File: USPT Nov 13, 1990

DOCUMENT-IDENTIFIER: US 4970154 A
TITLE: Method for inserting foreign genes into cells using pulsed radiofrequency

ABPL:
Disclosed are an apparatus and a method for the poration and fusion of cells using high-power radiofrequency electrical pulses. The electrodes of the apparatus can be hand held or part of integrated equipment with special containers for cells. The electrodes, which are positioned equidistant from each other, are attached to a high power function generator. The power function generator can apply a continuous AC electrical field and/or a high-power pulsed radiofrequency electrical field across the electrodes. The alternating electrical field induces cell congregation by the process of dielectrophoresis. The high-power pulsed radiofrequency electrical field porates or fuses the cells. The method has the ability to porate or fuse biological cells with a very high efficiency. The method can be used to fuse or porate a variety of cells including animal cells, human cells, plant cells, protoplasts, erythrocyte ghosts, liposomes, vesicles, bacteria and yeasts. The method has the unique ability to porate or fuse cells in very small or very large numbers. During the poration or fusions, a variety of chemical agents including DNA, RNA, antibodies, proteins, drugs, molecular probes, hormones, growth factors, enzymes, organic chemicals and inorganic chemicals can be introduced into these cells. The method can also be used to produce new biological species, to make hybridoma cells which produce animal or human monoclonal antibodies and to insert therapeutic genes into human cells which can be transplanted back into the human body to cure genetic diseases.

WEST

Help | Logout | Interrupt

Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences

Search Results -

Terms	Documents
(liposomes) same (electrical)	133

Database: US Patents Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: (liposomes) same (electrical) Clear

Search History

Today's Date: 1/22/2001

DB Name	Query	Hit Count	Set Name
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) same (electrical)	133	L3
USPT,JPAB,EPAB,DWPI,TDBD	(liposomes) same (electrical or iontophore$$$)	299	L2
USPT,JPAB,EPAB,DWPI,TDBD	liposomes same (electrical or iontophore$$$)	299	L1

WEST

Generate Collection

L6: Entry 2 of 18 File: USPT Jun 13, 2000

US-PAT-NO: 6074666
DOCUMENT-IDENTIFIER: US 6074666 A

TITLE: Liposome compositions of porphyrin photosensitizers

DATE-ISSUED: June 13, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Desai; Narendra Raghunathji	Danbury	CT	N/A	N/A
Agha; Bushra J.	Durham	NC	N/A	N/A
Kale; Kalidas Madhavrao	Harriman	NY	N/A	N/A

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
QLT Phototherapeutics, Inc.	N/A	N/A	N/A	CAX	03

APPL-NO: 8/ 489850
DATE FILED: June 13, 1995

PARENT-CASE:
This application is a continuation of application Ser. No. 07/832,542, filed Feb. 5, 1992, now abandoned.

INT-CL: [7] A61K 9/127, A61K 31/40
US-CL-ISSUED: 424/450
US-CL-CURRENT: 424/450
FIELD-OF-SEARCH: 424/450

REF-CITED:

U.S. PATENT DOCUMENTS

Search Selected Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	4776991	October 1988	Farmer et al.	514/832
☐	4880635	November 1989	Janoff et al.	424/450
☐	4913907	April 1990	Jori et al.	N/A
☐	4920143	April 1990	Levy et al.	N/A
☐	5010073	April 1991	Kappas et al.	514/410
☐	5270053	December 1993	Schneider et al.	N/A

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
2047969A	February 1992	CAX	
0451103A1	September 1991	EPX	
2256139	February 1992	GBX	

OTHER PUBLICATIONS

Kuzelova, K., et al., "Interactions of Dicarboxylic Porphyrins with Unilamellar Lipidic Vesicles: Drastic Effects of pH and Cholesterol in Kinetics," Biochemistry (1995) 34:11245-11255.
Ricchelli, F., et al., "Porphyrins as fluorescent probes for monitoring phase transitions of lipid domains in biological membranes. Factors influencing the microenvironment of haematoporphyrin and protoporphyrin in liposomes," Journal of Photochemistry and Photobiology B:Biology (1995) 29:65-70.
Scherphof, G., et al., "The Involvement of the Lipid Phase Transition in the Plasma-Induced Dissolution of Multilamellar Phosphatidylcholine Vesicles," Biochimica et Biophysica Acta (1979) 556:196-207.
Oku, N., et al., "Application of Long-Circulating Liposomes to Cancer Photodynamic Therapy," Biol Pharm Bull (1997) 20(6):670-673.
Richter, A.M., et al., "Liposomal Delivery of a Photosensitizer, Benzoporphyrin Derivative Monoacid Ring A (BPD), to Tumor Tissue in a Mouse Tumor Model," Photochemistry and Photobiology (1993) 57(6):1000-1006.
W.G. Love et al., "Liposome Association with Inflammatory Tissue", in Liposomes in Drug Delivery, Gregoriadis et al. eds., Chapter 11, pp. 149-188, Harwood Academic Publishers, 1993.
Ricchelli et al., New Directions in Photodynamic Therapy, SPIE 847: 101-106 (1987).
Zhou et al., Photochemistry and Photobiology, 48: 487-492 (1988).
Cohen et al., Arch. Biochem. & Biophys., 247: 57-61 (1986).
Margalit et al., Adv. Exp. Med. Biol., 193 (Methods Porphyrin Photosensit.), 303-11 (1985).
Johnson, et al., Photodynamic Therapy: Mechanisms II, SPIE: 266-280 (1990).
Milanesi et al., Br. J. Cancer, 61: 846-850 (1990).
Cuomo et al., Br. J. Cancer, 62: 966-970 (1990).
Milanesi et al., Int. J. Radiat. Biol., 55: 59-69 (1989).
Gantchev et al., Studia Biophysica, 131: 7-20 (1989).
Thomas et al., Biochemica et Biophysica Acta, 962: 297-307 (1988).
Firey et al., Photochemistry and Photobiology, 48: 357-360 (1988).
Sicuo et al., NATO ASI Ser., Ser. H, 15 (Photosensitization) 431-3 (1988.
Barel et al., Med. Biol., Environ., 14(1): 35-40 (1986).
Ricchelli et al., F.E.C.S. Int. Conf. Chem. Biotechnol. Act Nat. Prod., [Proc.], 3rd, 5: 241-4 (1985).
Parasassi et al., Inorganica Chemica Acta, 66: 137-139 (1982).
Davis et al., Laryngoscop, 100(7): 682-6 (1990) (CA 114(3): 20249p).
Poretz et al., Proc. SPIE-Int. Soc. Opt. Eng., (Photodyn. Ther.: Mech.) 1065: 197-203 (1989) (CA 111(15): 129891f).
Ricchelli et al., Proc. SPIE-Int. Soc. Opt. Eng., 847 (New Dir. Photodyn. Ther.): 101-106 (1988) (CA 109(20): 176210b).
Morgan et al., Proc. SPIE-Int. Soc. Opt. Eng., 847 (New Dir.Photodyn. Ther.): 180-196 (1988) (CA 108(23): 200892d).
Cozzani et al., Med. Biol. Environ., 14(1): 73-76 (1986) (CA 107(3): 20038z).
Cozzani et al., Chem. Biol. Interact., 53(1-2): 131-43 (1985) (CA 103(5): 34264z).

Grossweiner L., Proc. SPIE-Int. Soc. Opt. Eng., 712 (Lasers Med.) 149-53 (1987) (CA 106(23): 192002d).
Grossweiner, et al., Adv. Exp. Med. Biol., 193 (Methods Porphyrin Photosensit.): 181-92 (1985) (CA 105(9): 75058v).
Facchini et al., Med. Biol. Environ., 12(1): 469-74 (1984) (CA 102(19): 163061j).
Spikes, J., Adv. Exp. Med. Biol., 160: (Porphyrin Photosensit.): 181-92 (1983) (CA 98(15): 122156z).

ART-UNIT: 165
PRIMARY-EXAMINER: Kulkosky; Peter F.
ATTY-AGENT-FIRM: Morrison & Foerster

ABSTRACT:

Liposomal pharmaceutical formulations incorporating porphyrin photosensitizers useful for photodynamic therapy or diagnosis of malignant cells. The liposomal formulations comprise a porphyrin photosensitizer, particularly the hydro-mono benzoporphyrins (BPD) having light absorption maxima in the range of 670-780 nanometers, a disaccharide or polysaccharide and one or more phospholipids.

12 Claims, 10 Drawing figures

L6: Entry 9 of 18 File: USPT Jan 13, 1998

DOCUMENT-IDENTIFIER: US 5707608 A
TITLE: Methods of making liposomes containing hydro-monobenzoporphyrin photosensitizer

BSPR:
The invention relates to improved pharmaceutical compositions comprising liposomes incorporating porphyrin photosensitizers and methods for making these liposomes. Specifically, the invention is directed to pharmaceutical liposome compositions comprising a hydro-monobenzo-porphrin photosensitizer and a mixture of phospholipids comprising egg phosphatidyl glycerol ("EPG") and dimyristoyl phosphatidyl choline ("DMPC") in a photosensitizer:phospholipid molar ratio of about 1:7.0 or more phospholipid. The liposomes are made in such a way that the particle size range is about 150 to 300 nm.

BSPR:
Thus, there remains a need for a large-scale method to produce DMPC/EPG liposomes containing a photosensitizer in small enough particle sizes that large quantities of pharmaceutical compositions containing the liposomes are easily aseptically filtered through standard 0.22 .mu.m sterilizing filters in an efficient manner and without the need for preparing the synthetic lipids of Kappas et al.

BSPV:
c. hydrating the lipid film with an aqueous solution at a temperature below 30.degree. C., to form coarse liposomes containing a photosensitizer-phospholipid complex; and

DEPR:
In an especially preferred embodiment, the particular combination of the phospholipids, DMPC and EPG, and a disaccharide or polysaccharide form a liposomal composition having liposomes of a particularly narrow particle size distribution. When the process of hydrating a lipid film is prolonged, larger liposomes tend to be formed, or the photosensitizer can even begin to precipitate. The addition of a disaccharide or polysaccharide provides instantaneous hydration and the largest surface area for depositing a thin film of the drug-phospholipid complex. This thin film provides for faster hydration so that, when the liposome is initially formed by adding the aqueous phase, the liposomes formed are of a smaller and more uniform particle size. This provides significant advantages in terms of manufacturing ease.

DEPR:
Four batches of BPD-MA liposome compositions, each having the same photosensitizer/DMPC-EPG lipid molar ratio (1.05:3:5), were prepared using different film hydration temperatures. Data for these four batches, presented below in Table 5, were compared to demonstrate the relationship of potency loss and film hydration temperature.

CLPV:
c. hydrating said photosensitizer:phospholipid complex with an aqueous solution at a temperature below the glass transition temperature of the photosensitizer:phospholipid complex to form coarse liposomes containing said photosensitizer-phospholipid complex; and

ORPL:
Ricchelli, "Liposomes as carriers of hydrophobic photosensitizers in vivo: increased selectivity of tumor targeting," New Directions in Photodynamics Therapy, 847:101-106 (1987).

L6: Entry 14 of 18 File: USPT Jan 11, 1994

DOCUMENT-IDENTIFIER: US 5277913 A
TITLE: Liposomal delivery system with photoactivatable triggered release

DEPR:
FIG. 4 shows the release kinetics of liposome entrapped glucose after irradiation of 8:1 PlasPPC/DPPC liposomes containing ZnPc as the photosensitizer ([lipid]/[ZnPc]>10.sup.4). Release rates were determined at 15.degree. C., at which temperature the vesicles are in the gel phase, and at 37.degree. C., where a more fluid bilayer predominates. After 60 minutes of irradiation, less than 20% of the entrapped glucose has been released at 15.degree. C., compared with 62% at 37.degree. C. Photoirradiation of the liposomes therefore enhances glucose release at the physiological temperature of 37.degree. C. which is found in a human body. Dark leakage from ZnPc/PlasPPC/DPPC liposomes was also measured at both temperatures. After 60 minutes at 15.degree. and 37.degree. C., glucose release was found to be 4 and 30%, respectively. Hence, irradiation of the liposomes produces a substantial increase in glucose release of the ZnPC/PlasPPC/DPPC vesicles.

WEST

End of Result Set

Generate Collection

L6: Entry 18 of 18 File: EPAB Nov 2, 1993

DOCUMENT-IDENTIFIER: US 5257970 A
TITLE: In situ photodynamic therapy

FPAR:
The process of photodynamic therapy (PDT) is conducted by the step of: 1) separately encapsulating at least one activation component for said photodynamic therapy process in a liposome; 2) injecting a photosensitizer into a human or animal host; 3) injecting the liposome encapsulated components systemically into the same human or animal host; and 4) heating the site of the tumor to melt the liposome encapsulated components to permit mixing of the activation components. The mixing of the activation components can result in: a) energy transfer to the previously injected photosensitizer; b) emission of light and absorption of said light by the previously injected photosensitizer; and c) direct formation of at least one cytotoxic species that functions against the tumor. The heating of the site of the tumor is accomplished by one of the following methods: laser, ultra sound, radio-frequency or microwave frequency. Photofrin photosensitizer is a preferred photosensitizer.